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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,648	06/24/2005	Franz Guck	RO4077US(#90568)	8878

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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,648	GUCK ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending. In a preliminary amendment on June 24, 2005 Applicants amended claims 1-13 and submitted new claims 14-18.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating allergic diseases of the respiratory tract selected from asthma and allergic rhinitis by the administration of formulations comprising a glucocorticoid, does not reasonably provide enablement for the treatment of all allergic diseases with any kind of medicinal agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue

experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims

Applicants' claim is broad regarding the disease being treated as well as the medicinal agent present in the composition administered to treat the disease. Applicants' claim does not limit "medicinal agents" to glucocorticoids.

Nature of the invention/State of the Prior Art

Applicants' invention is directed to suspension aerosol formulations comprising (a) isobutane propellant, (b) lecithin as the surfactant, and (c) medicinal agents. The art recognizes that glucocorticoids & corticosteroids (e.g. budesonide), beta-adrenergic agonists (e.g. formoterol), methylxanthines (e.g. theophylline), leukotriene modifiers (e.g. montelukast), anticholinergics (e.g. ipratropium), and immunomodulators (i.e. omalizumab) are indicated for the treatment of allergic respiratory diseases, such as

asthma (Merck Home Edition articles, entitled, "Asthma" and "Allergic Bronchopulmonary Aspergillosis" –accessed on December 22, 2008 from the following online websites: www.merck.com/mmhe/print/sec04/ch044/ch044a.html or www.merck.com/mmhe/print/sec04/ch051/ch051da.html). Allergic conjunctivitis is treated by the administration of an antihistamine, such as naphazoline, via an eye drop (Merck Home Edition article entitled, "Allergic Conjunctivitis"-accessed on December 22, 2008 from www.merck.com/mmhe/print/sec20/ch0229/ch229d.html). Thus, the prior art does not recognized that any medicinal agent is suitable for the treatment of allergic diseases, but rather that specific medicinal agents are required to treat various allergic diseases. Furthermore, the prior art recognizes that glucocorticoids are not indicated for the treatment of all allergic diseases (e.g. allergic conjunctivitis). Thus, to practice the full scope of Applicants' claimed method of treating allergic diseases, an ordinary skilled artisan would have to rely upon an unduly burdensome quantity of experimentation to ascertain which drugs and in what amounts are suitable to treat said diseases with any medicinal agent or solely with glucocorticoids.

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970).

Guidance/Working Examples

The only guidance provided by Applicants is the teaching that formulations of the instant application are suitable in the treatment of allergic diseases, such as asthma and allergic rhinitis.

In conclusion, while being enabling for a method of treating allergic diseases of the respiratory tract selected from asthma and allergic rhinitis by the administration of formulations comprising a glucocorticoid, does not reasonably provide enablement for the treatment of all allergic diseases by the administration of any kind of medicinal agent or the administration of glucocorticoids alone.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4 and 6-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-4 recites the limitation "glucocorticoid" in line 3. There is insufficient antecedent basis for this limitation in the claim. There is no mention of the term "glucocorticoid" in parent claim 1, from which claims 3-4 directly depend.

Claim 6 recites the limitation "beclomethasone" in line 3 and "soybean lecithin" in lines 3-4. There is insufficient antecedent basis for this limitation in the claim. There is no mention of the terms "beclomethasone" or "soybean lecithin" in parent claim 1, from which claim 6 directly depends.

Claim 7 recites the limitation "budesonide" in lien 3 and "soybean lecithin" in line 3. There is insufficient antecedent basis for these limitations in the claim. There is no mention of the terms "budesonide" or "soybean lecithin" in parent claim 1, from which claim 7 directly depends.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over DE19911064 (DE'064) (IDS reference) in view of Keller et al. (U.S. Patent No. 6,461,591).

Applicant Claims

Applicants claim controlled dosage suspension aerosols comprising (a) at least one suspended medicinal agent, isobutane as the propellant, and lecithin as the surface-active agent.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

DE '064 teaches **metered dose inhalers containing aerosol suspension formulations comprising bronchiolytic active agents and isobutane that has been liquefied under pressure as the propellant** (English abstract; col. 4, lines 38-43). The bronchiolytic active agents are selected from the group of **glucocorticoids or derivatives thereof**, such as **budesonide, prednisone, dexamethasone, beclomethasone**, etc. (English abstract; col. 2, lines 31-41; and claims 2-15). **Suitable amounts of isobutane propellant range from 97-99.4%** (col. 2, lines 45-46; Example 6: col. 4, lines 5-12; claim 13). **Suitable amounts of glucocorticoid range from 0.10-1.00%** (Example 6: col. 4, lines 5-11). **Suitable amounts of surfactant** (e.g. Span 85) are **0.50-5.00%** (Example 6; and claims 3-15). Combinations of glucocorticoids may also be used (claims 4 and 8). The invented aerosol suspension formulations are **indicated for the treatment**

of allergic diseases, such as asthma and allergic rhinitis (col. 4, lines 44-49 and claims 16-17). **The suspension aerosol formulation is filled into the MDI via the valve, while under pressure and has a temperature from -8 C to -10 C (col. 4, lines 38-41). After filling of the MDI with the aerosol suspension formulation, the valve is cleaned by the passage of additional propellant** (col. 4, lines 41-43).

Keller teaches solution and suspension aerosol formulations and that the use of surface-active agents (i.e. surfactants) is frequently indicated for suspension formulations (title; abstract; col. 10, lines 7-20). Typical suitable surfactants include **soya lecithin and sorbitan trioleate** (i.e. Span 85), which are preferred conventional surfactants (col. 7, lines 9-10 and col. 10, lines 7-20). Thus, soya lecithin and sorbitan trioleate are art-recognized functionally equivalent surfactants.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

DE '064 lacks the teaching of formulations wherein the surfactant is lecithin (e.g. soya lecithin), the explicit teaching of glucocorticoid/surfactant ratio and the

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious at the time of the instant invention to substitute sorbitan trioleate (i.e. Span85) for soya lecithin, because both sorbitan trioleate and soya lecithin are art recognized functionally equivalent surfactants conventionally used in suspension aerosol formulations. An ordinary skilled artisan would have been motivated to substitute sorbitan trioleate with soya lecithin, because both surfactants are

functionally equivalent and an ordinary skilled artisan would have had a reasonable expectation of successfully preparing suitable suspension aerosol formulations with either surfactant. Furthermore, an ordinary skilled artisan would have been motivated to substitute sorbitan trioleate for lecithin, because lecithin is also a preferred conventional surfactant for suspension aerosol formulations. Regarding the ratio of surfactant and drug, the amount of glucocorticoid and surfactant taught by DE '064 as being suitable encompasses the specific ranges recited by Applicants in claims 14-15. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Regarding the property of controlled release, because the prior art formulations comprises essentially the same components, these formulations would necessarily exhibit the same or substantially similar release properties. Applicants' tabulated data on page 4 of the specification is noted, which compares formulations comprising glucocorticoids and surfactants selected from oleic acid, Span 85, and soybean lecithin in ratios of glucocorticoid to surfactant of 100:1 (oleic acid only) to 1:0.5 (soybean lecithin only). Applicants' data does not overcome the instant rejection because it is not commensurate in scope with Applicants' claims. Claims 1, 5, 8-18 are not limited to formulations wherein the medicinal agent is a glucocorticoid, and are thus not commensurate in scope

with Applicants' data. Claims 3-4 and 6-7 are not limited to formulations having a glucocorticoid/soybean lecithin ratio of 1:0.5, 1:1, or 1:2, and are thus not commensurate in scope with Applicants' data. Furthermore, the prior art is strongly suggestive of the interchangeability of sorbitan trioleate (i.e. Span 85) and lecithin, such that there is a strong motivation to substitute sorbitan trioleate for soybean lecithin and obtain Applicants' claimed formulations, regardless of Applicants' data.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

Claims 1-18 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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